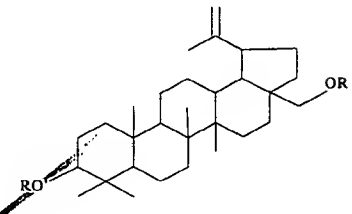
WHAT IS CLAIMED:

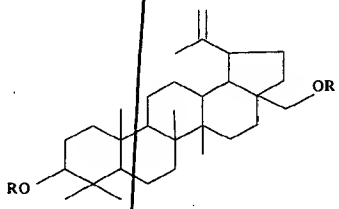
1. A diether having the formula:



wherein R is an alkyl group.

2. A diether according to claim 1, wherein R is methyl.

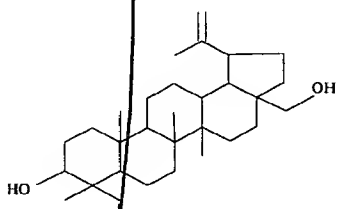
3. A method of synthesizing a diether having the formula:



wherein R is alkyl,

said method comprising:

providing a dialcohol having the formula:



and

alkylating the dialcohol with a nitrile having the formula:

R-C≡N

under conditions effective to form the diether.

15 4. A method according to claim 3, wherein R is methyl.

16 5. A method according to claim 3, wherein the dialcohol and the nitrile, respectively, are present in a mole ratio of from about 1:20 to about 1:60.

17 6. A method according to claim 3, wherein said alkylating is carried out at a temperature of from about 30°C to about 70°C.

Sub D2 7. A method of preparing betulonic aldehyde comprising:

oxidizing betulinol with chromium anhydride in acetone in the presence of sulfuric acid under conditions effective to produce betulonic aldehyde.

19 8. A method according to claim 7, wherein the betulinol and acetone, respectively, are present in a weight ratio of from about 1:100 to about 1:110.

20 9. A method according to claim 7, wherein the chromium anhydride and sulfuric acid, respectively, are present in a molar ratio of from 9:10 to about 10:9.

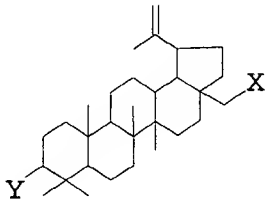
Sub D3 10. A method according to claim 7 further comprising, after said oxidizing:

cooling the reaction mixture; and

adding water to the reaction mixture, whereby a sediment containing betulonic aldehyde forms.

11. A method according to claim 10 further comprising:
recrystallizing the sediment.

12. A compound having the formula:



wherein

X or Y is a -peptide-Q moiety and the other of X and Y is a hydroxy group, an alkoxy group, an alkanoyloxy group, or a -peptide-Q moiety;

Q is a hydroxy group, a $-NHNH_2$ moiety, an $-NHNH-C(O)CH_2Hal$ moiety, an -antibody-OH moiety, or an -NHNH-C(O)-antibody-OH moiety; and

Hal is a halogen.

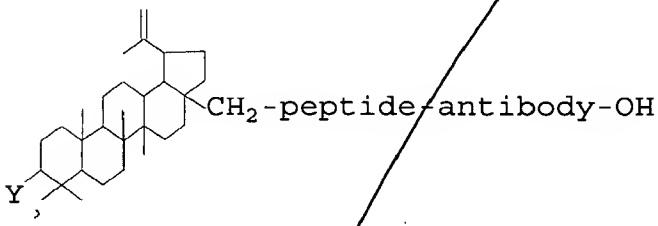
13. A compound according to claim 12, wherein -peptide- is a pentapeptide.

14. A compound according to claim 13, wherein the pentapeptide is -Gly-Ala-Leu-Gly-Leu-.

15. A compound according to claim 12, wherein -peptide- is a tetrapeptide.

16. A compound according to claim 15, wherein the tetrapeptide is -Leu-Ala-Leu-Ala-.

17. A method of producing a betulinol-antibody conjugate having the formula:



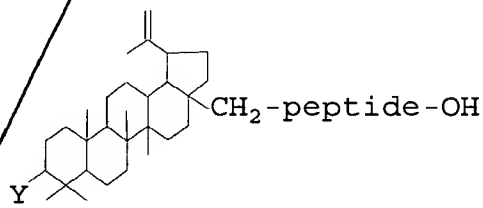
V

wherein

Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group,

said method comprising:

providing a betulinol peptide having the formula:



VI

and

converting the betulinol peptide with an antibody having the formula H-antibody-OH under conditions effective to produce the betulinol-antibody conjugate.

24 23

18. A method according to claim 17, wherein -peptide- is a pentapeptide.

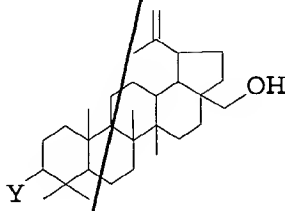
19. A method according to claim 18, wherein the pentapeptide is -Gly-Ala-Leu-Gly-Leu-.

20. A method according to claim 17, wherein -peptide- is a tetrapeptide.

21. A method according to claim 20, wherein the tetrapeptide is -Leu-Ala-Leu-Ala-.

22. A method according to claim 17, wherein said providing the betulinol peptide comprises:

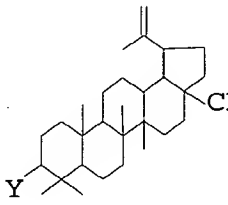
providing a compound having the formula:



and

converting the compound with a peptide having the formula H-peptide-OH under conditions effective to produce the betulinol peptide.

23. A method of producing a betulinol-antibody conjugate having the formula:

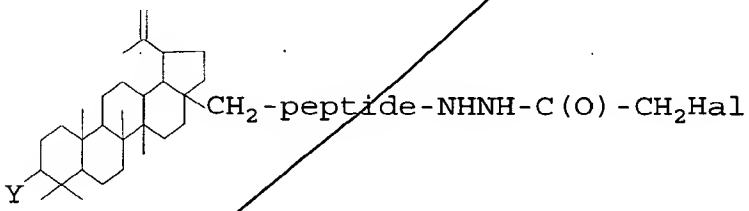


wherein

Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group,

said method comprising:

providing a haloacetylhydrazide having the formula:



wherein

Hal is a halogen

and

converting the haloacetylhydrazide with an antibody having the formula H-antibody-OH under conditions effective to produce the betulinol-antibody conjugate.

24. A method according to claim 23, wherein Hal is I.

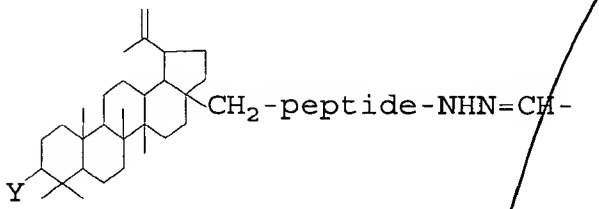
25. A method according to claim 23, wherein -peptide- is a pentapeptide.

26. A method according to claim 25, wherein the pentapeptide is -Gly-Ala-Leu-Gly-Leu-.

27. A method according to claim 23, wherein -peptide- is a tetrapeptide.

28. A method according to claim 27, wherein the tetrapeptide is -Leu-Ala-Leu-Ala-.

at least one A is a moiety having the formula:



and

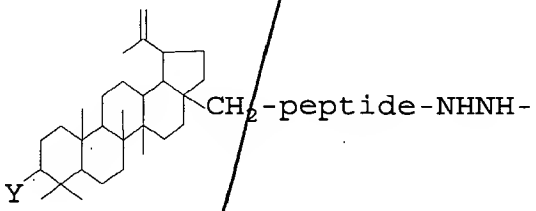
converting the betulinol-bound carrier molecule with the antibody under conditions effective to produce the betulinol-antibody conjugate.

36. A betulinol-antibody conjugate having the formula:

HO-antibody-spacer-$(A)_n$

wherein

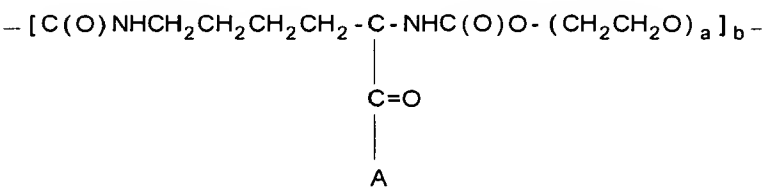
A is a moiety having the formula:

an 

Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group; and

n is an integer from 1 to 100.

37. A betulinol-antibody conjugate according to claim 36, wherein -spacer-$(A)_n$ has the formula:



wherein

a is an integer from 1 to 100 and

b is an integer equal to n.

Sub D10

38. A betulinol-antibody conjugate according to claim 36, wherein spacer is a diamine derivative of polyethylene glycol having 2-(pyridyldithio)-propionyl and N-hydroxysuccinimide ester groups bonded thereto.

39. A betulinol-antibody conjugate according to claim 36, wherein spacer is a branched form of polyethylene glycol propionic acid N-hydroxysuccinimide ester.

13 12

40. A betulinol-antibody conjugate according to claim 39, wherein the branched form of polyethylene glycol propionic acid N-hydroxysuccinimide ester is a monomethoxypoly(ethylene glycol)-propionic acid N-hydroxysuccinimide ester.

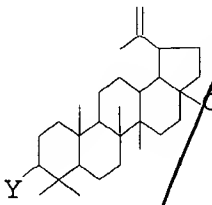
Sub D11

41. A method of producing a betulinol-antibody conjugate having the formula:

HO-antibody-spacer-$(A)_n$

wherein

A is a moiety having the formula:



Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group; and

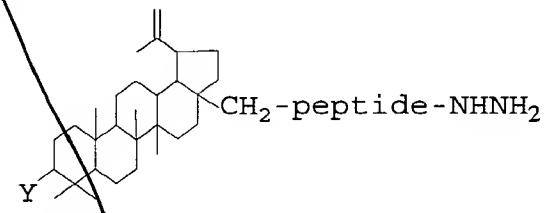
n is an integer from 1 to 100,

said method comprising:

providing a crosslinker having a first reactive terminus and one or more second reactive termini;

reacting an antibody with the first reactive terminus; and

reacting a hydrazide having the formula:



with one or more of the one or more second reactive termini under conditions effective to produce the betulinol-antibody conjugate.

42. A method according to claim 41, wherein the first reactive terminus is selected from the group consisting of a hydroxy group, an aldehyde group, and a carboxyl group.

43. A method according to claim 41, wherein each of the one or more second reactive termini are independently selected from the group consisting of a hydroxy group, an aldehyde group, and a carboxyl group.

44. A method according to claim 41, wherein -spacer-$(A)_n$ has the formula:

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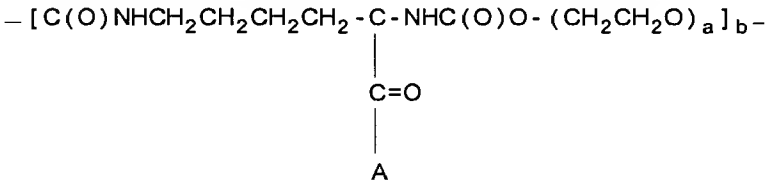


wherein

a is an integer from 1 to 100 and

b is an integer equal to n.

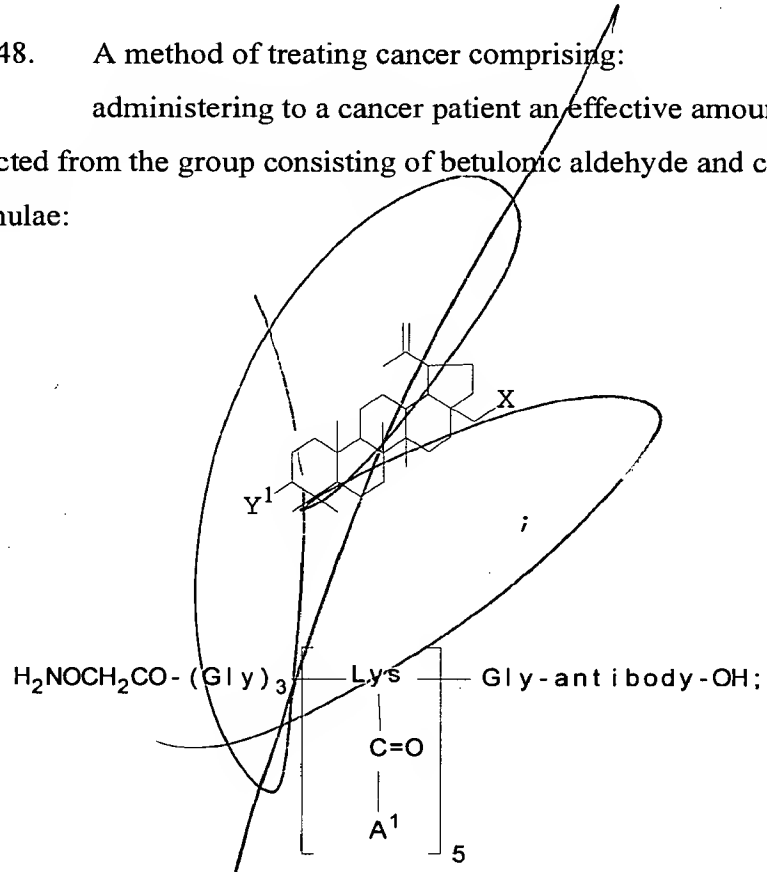
45. A method according to claim 41, wherein spacer is a diamine derivative of polyethylene glycol having 2-(pyridyldithio)-propionyl and N-hydroxysuccinimide ester groups bonded thereto.

46. A method according to claim 41, wherein spacer is a branched form of polyethylene glycol propionic acid N-hydroxysuccinimide ester.

47. A method according to claim 46, wherein the branched form of polyethylene glycol propionic acid N-hydroxysuccinimide ester is a monomethoxypoly(ethylene glycol)-propionic acid N-hydroxysuccinimide ester.

48. A method of treating cancer comprising:

administering to a cancer patient an effective amount of a compound selected from the group consisting of betulonic aldehyde and compounds having the formulae:



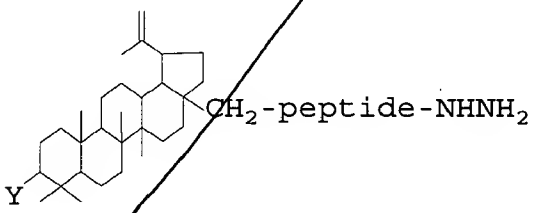
and

HO-antibody-spacer-$(A^2)_n$

wherein

29. A method according to claim 23, wherein said providing a haloacetylhydrazide comprises:

providing a hydrazide having the formula:



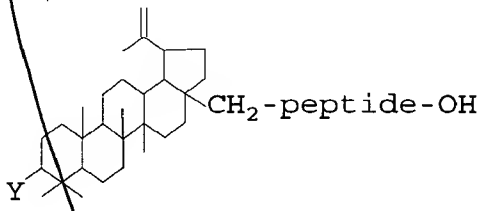
X

and

converting the hydrazide with a p-nitrophenyl haloacetate under conditions effective to produce the haloacetylhydrazide.

30. A method according to claim 29, wherein said providing a hydrazide comprises:

providing a betulinol peptide having the formula:



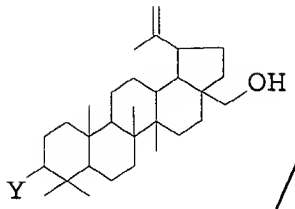
X1

and

converting the betulinol peptide with hydrazine hydrate under conditions effective to produce the hydrazide.

31. A method according to claim 30, wherein said providing the betulinol peptide comprises:

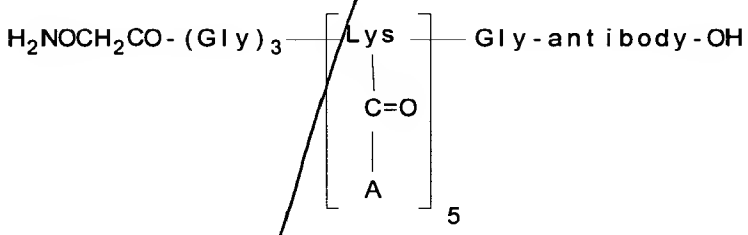
providing a compound having the formula:



and

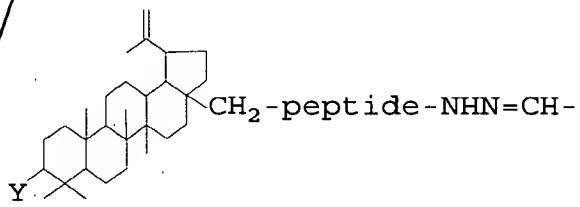
converting the compound with a peptide having the formula H-peptide-OH under conditions effective to produce the betulinol peptide.

32. A betulinol-antibody conjugate having the formula:



wherein

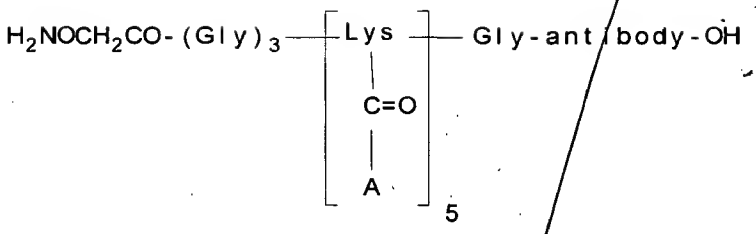
A are independently selected from a -CHO group or a moiety having the formula:



provided that at least one of A is not -CHO; and

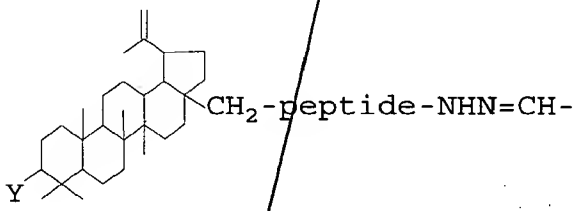
Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group.

33. A method of producing a betulinol-antibody conjugate having the formula:



wherein

A are independently selected from a -CHO group or a moiety having the formula:

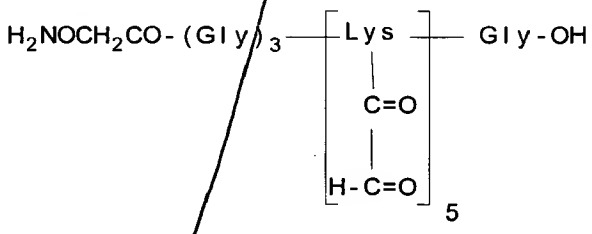


provided that at least one of A is not -CHO; and

Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group,

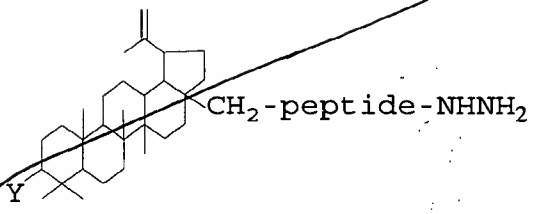
said method comprising:

providing a carrier molecule having the formula:



and

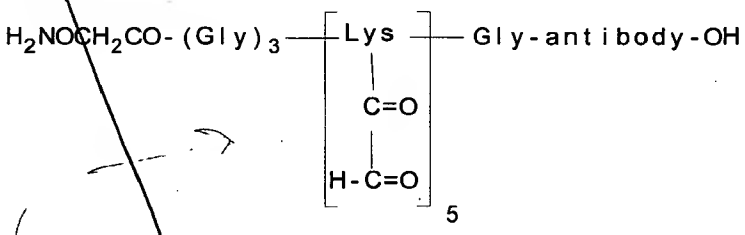
converting the carrier molecule with a hydrazide having the formula:



and an antibody having the formula H-antibody-OH under conditions effective to produce the betulinol-antibody conjugate.

34. A method according to claim 33, wherein said converting the carrier molecule comprises:

reacting the carrier molecule with the antibody under conditions effective to produce an antibody-bound carrier molecule having the formula:

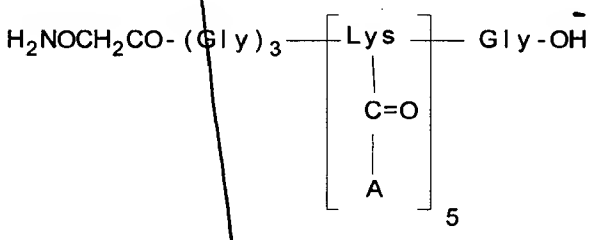


and

converting the antibody-bound carrier molecule with the hydrazide under conditions effective to produce the betulinol-antibody conjugate.

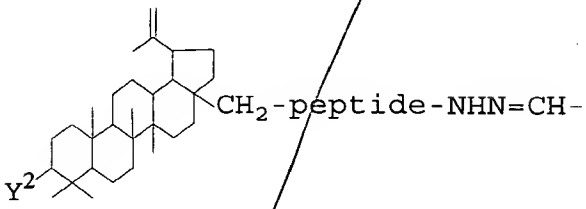
35. A method according to claim 33, wherein said converting the carrier molecule comprises:

reacting the carrier molecule with the hydrazide under conditions effective to produce a betulinol-bound carrier molecule having the formula:



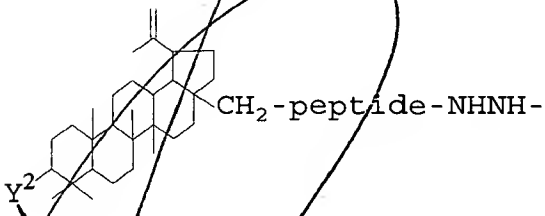
wherein

A^1 is a moiety having the formula:



;

A^2 is a moiety having the formula:



;

n is an integer from 1 to 100;

X and Y^1 are each independently selected from the group consisting of a hydroxy group, an alkoxy group, an alkanoyloxy group, and a -peptide-NHNH-C(O)-antibody-OH moiety;

Y^2 is selected from the group consisting of a hydroxy group, an alkoxy group, and an alkanoyloxy group; and

HO-antibody-H is an antibody targeted to a site to be treated in the patient.

49. A method according to claim 48, wherein the compound is betulinol diacetate.

50. A method according to claim 48, wherein the compound is betulonic aldehyde.

51. A method according to claim 50, wherein the compound is betulinol dimethyl diether.